A Quality System Approach to Research Integrity

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3 JUN 2024
Athens, 8th WCRI

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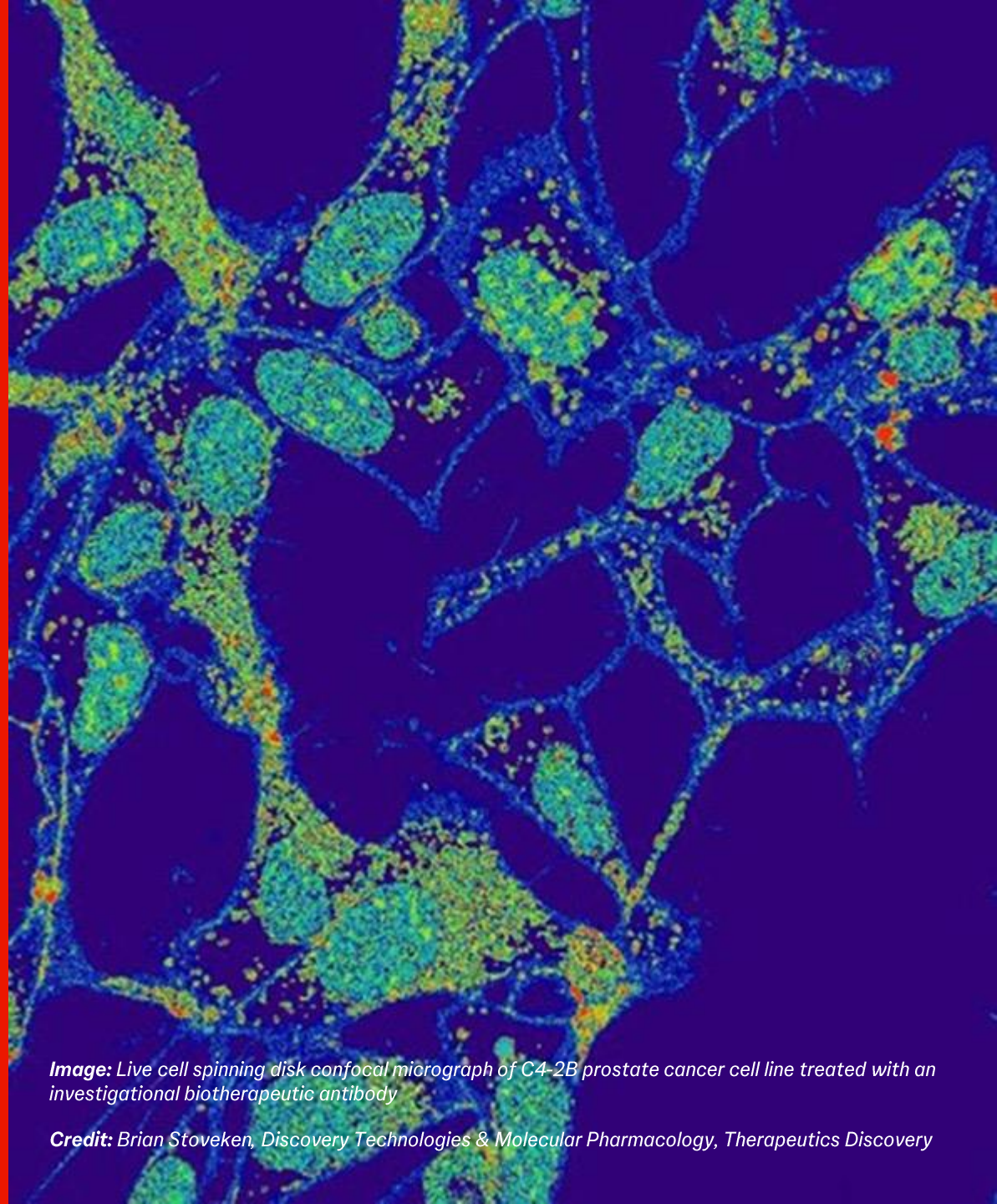

Image: *Live cell spinning disk confocal micrograph of C4-2B prostate cancer cell line treated with an investigational biotherapeutic antibody*

Credit: *Brian Stoveken, Discovery Technologies & Molecular Pharmacology, Therapeutics Discovery*

Agenda

Disclaimer:
'The views expressed in this presentation are solely those of the individual authors, and do not necessarily reflect the views of their employers'.

- Introduction
- Research Integrity Risks in context of Industry Preclinical Research
- Journey to implement Quality System in Discovery and Preclinical since 2010
  - Approach
  - Key success factors
  - Characteristics of a mature Quality System

“We believe our first responsibility is to the patients, doctors and nurses, to mothers and fathers and all others who use our products and services.”

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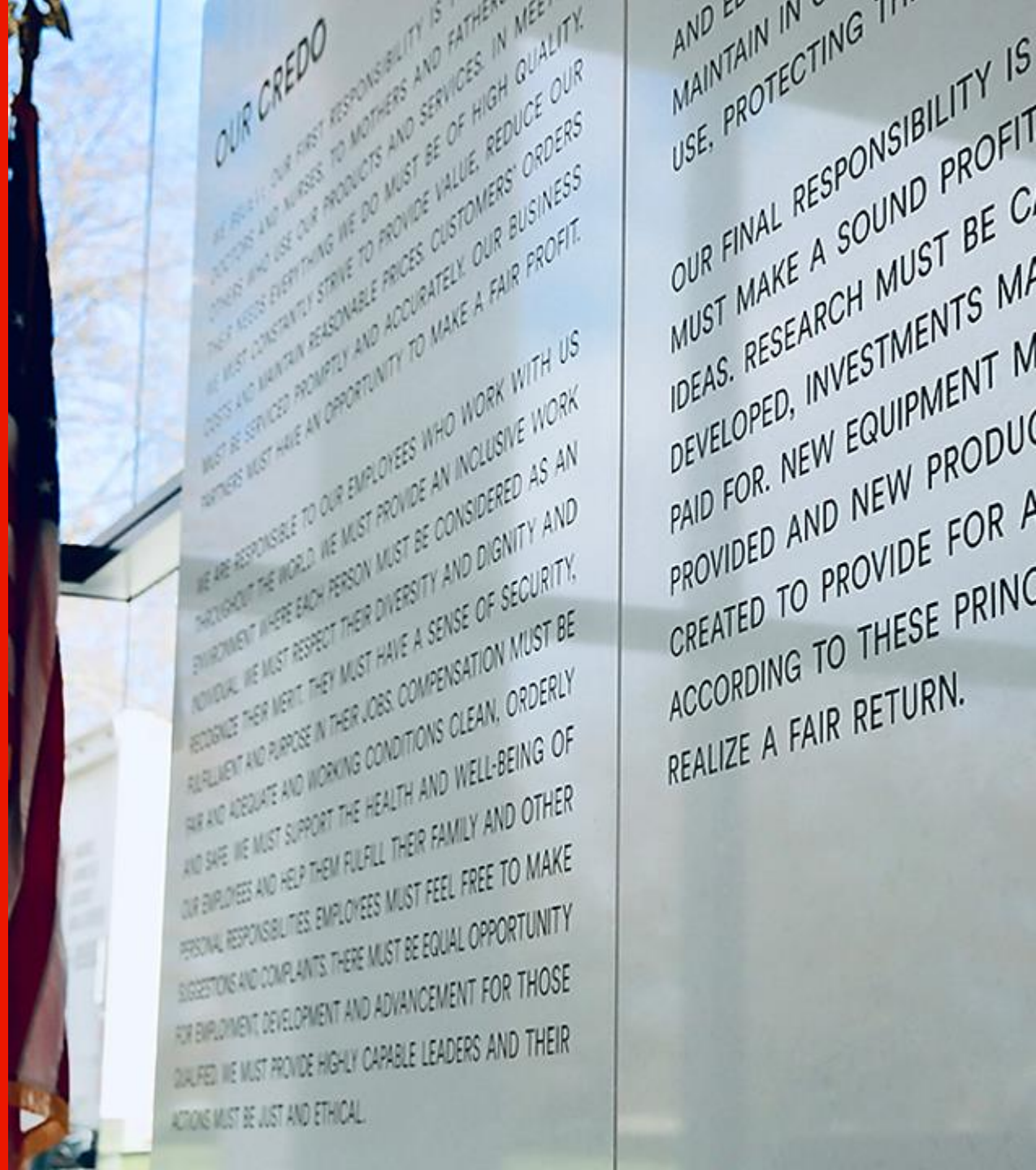
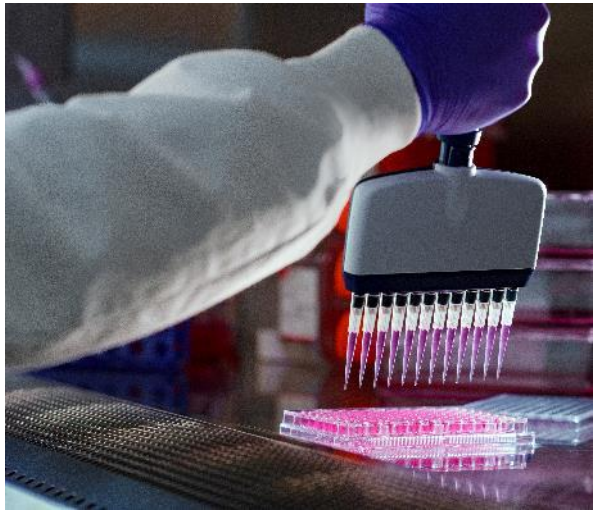


Johnson&Johnson

Our unique focus

An exclusive focus on healthcare empowers us to tackle the world's toughest health challenges.
We innovate across the full spectrum of healthcare solutions today to uniquely position us for the breakthroughs of tomorrow.

J&J Innovative Medicine



Leading where medicine is going.

Patients will always inform and inspire our science-based innovations, which continue to change and save lives. Applying rigorous science with compassion, we will continue to confidently address the most complex diseases of our time and unlock the potential medicines of tomorrow.

J&J MedTech

Innovating at the intersection of biology and technology.

Together, we will continue to develop smarter, less invasive, more personalized solutions to tackle the leading causes of mortality and the most complex diseases around the world.

Using our size and scale to change and save lives

45,600
Dedicated employees worldwide

13,000+
Scientists and researchers globally

179/13
External/internal manufacturing sites

$11.9B
Invested in research and development (R&D) in 2023[1]

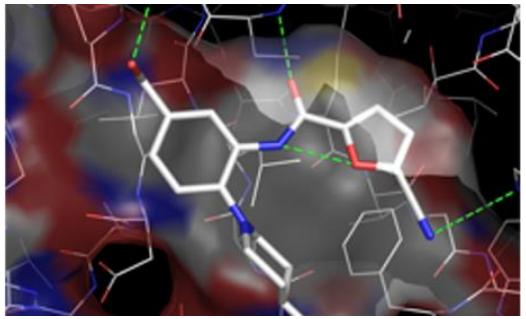
$54.8B
2023 Total worldwide sales[2]

#2
Ranked in the Access to Medicines Index 2022[3]

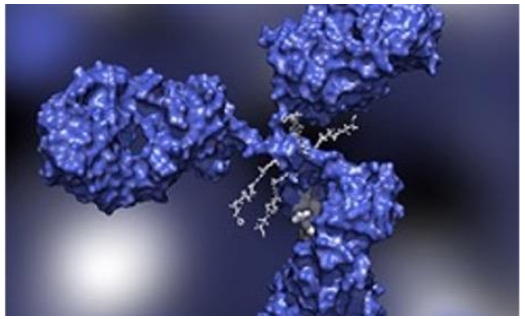
[1]https://www.investor.jnj.com/files/doc_financials/2023/q4/form-10-k-2023-final.pdf
[2]https://www.investor.jnj.com/files/doc_financials/2023/q4/Earnings-Infographic-4Q2023.pdf
[3]https://accesstomedicinefoundation.org/medialibrary/companies/221110_1_03-atmi22_rc-v1-jnj.pdf

Quality starts within Discovery

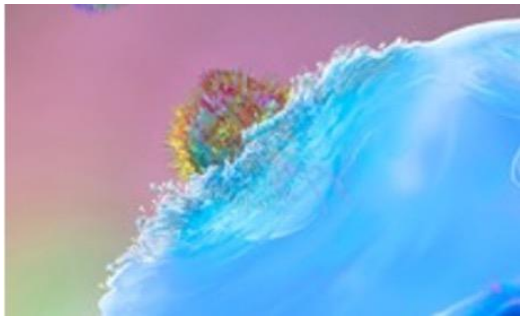
Scope of
Discovery Data Integrity (DDI)
Quality system



Small molecules



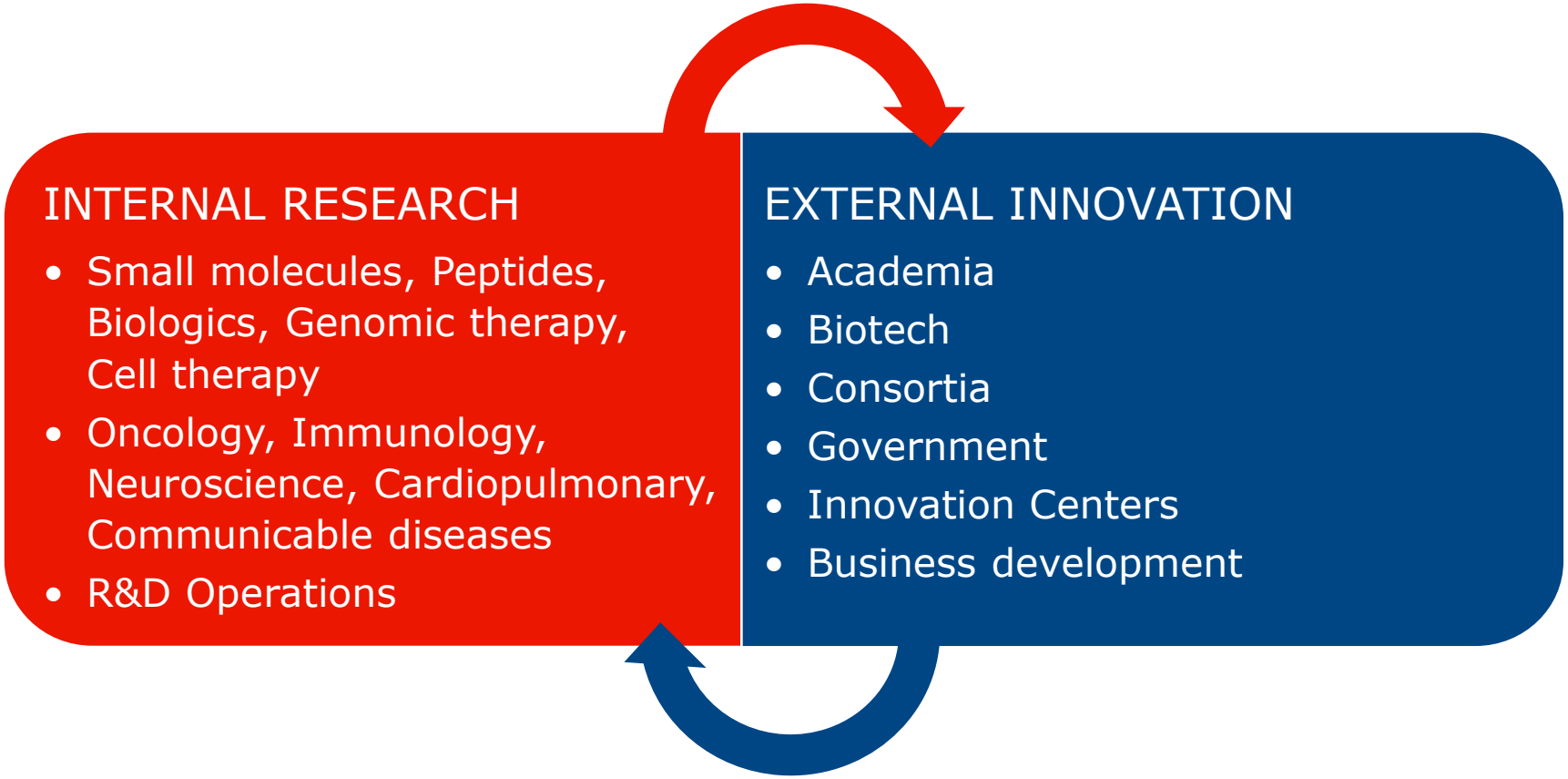
Protein therapeutics



Cell therapies

Gene/RNA therapies

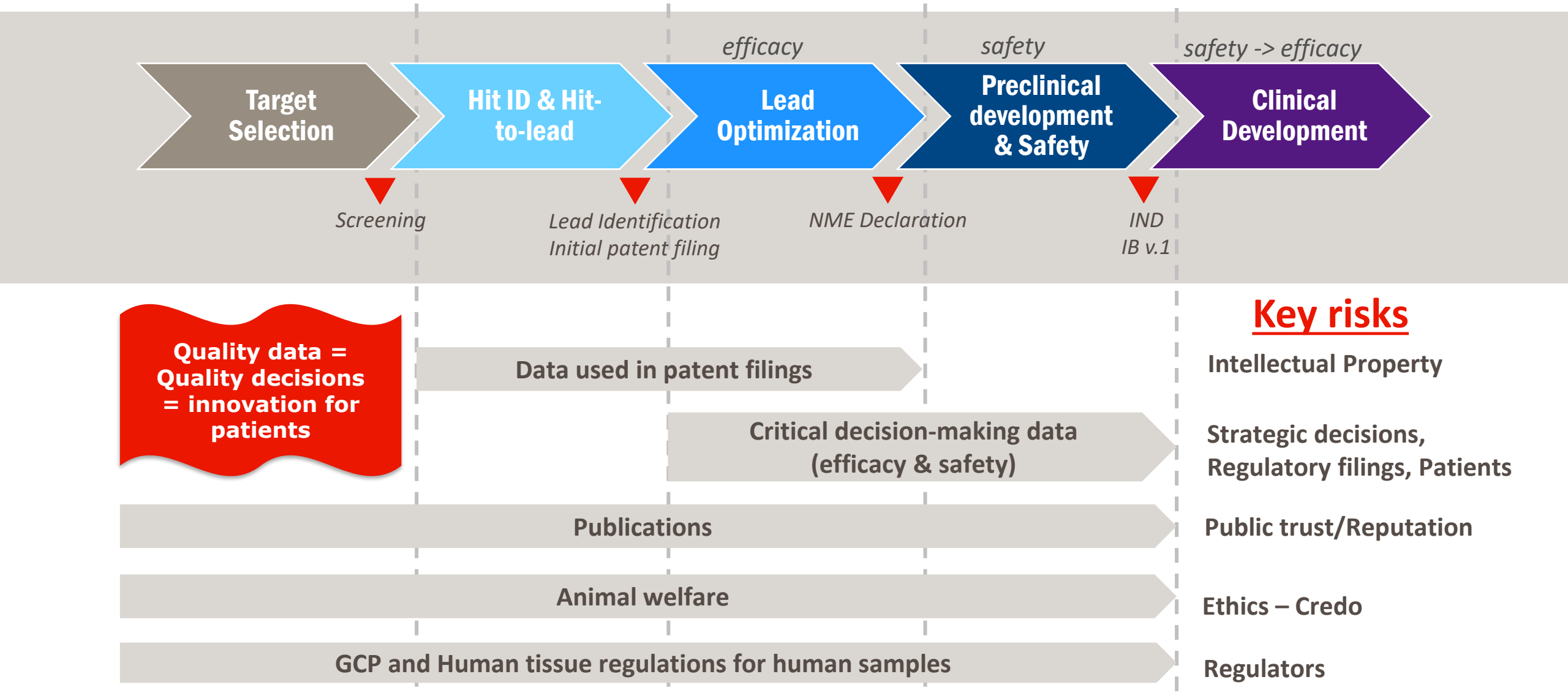
Internal Scientific Strength, External Innovation



How to Safeguard Research Integrity?

- Large internal organization with complex structure
- Multiple fast changing external collaborations in different settings (contracts)
- Early discovery to preclinical development
- Highly diverse scientific disciplines, techniques, modalities

Risks related to Research Integrity



The Basics

Focus on Data Quality

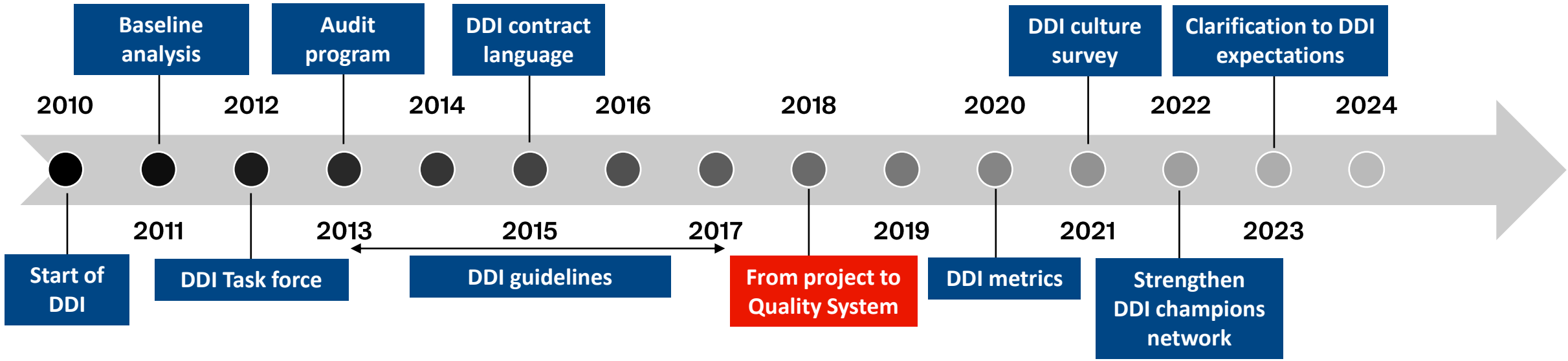
Data Traceability

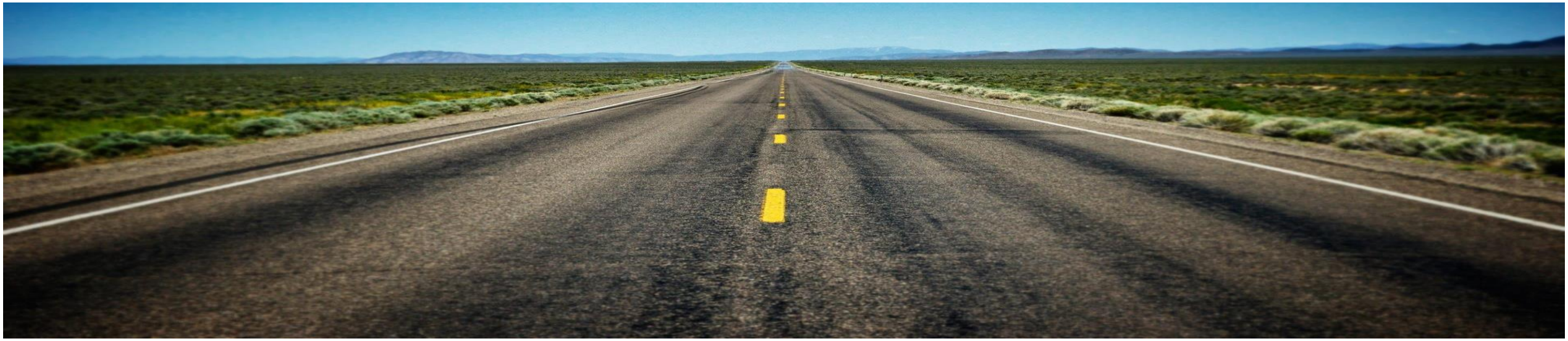
- **Ensure robust documentation** that can stand the test of time and allows reconstruction

Data Integrity

- **Right checks and balances** (e.g. automated calculation steps, adequate review) to **ensure reported outcomes are trustworthy**
- **Avoid** (perception of) **bias**: e.g set upfront exclusion criteria, blinding, randomization, consult biostatisticians as needed…

Discovery Data Integrity (DDI) Journey





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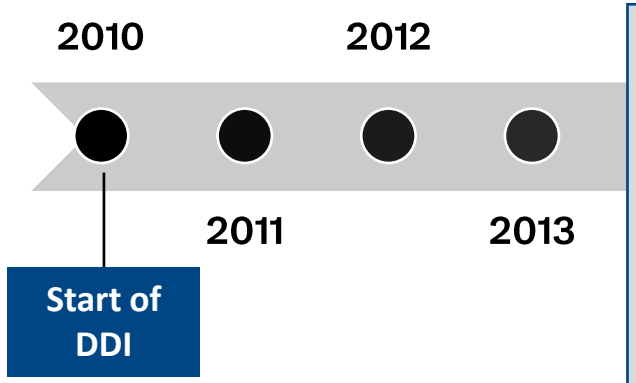
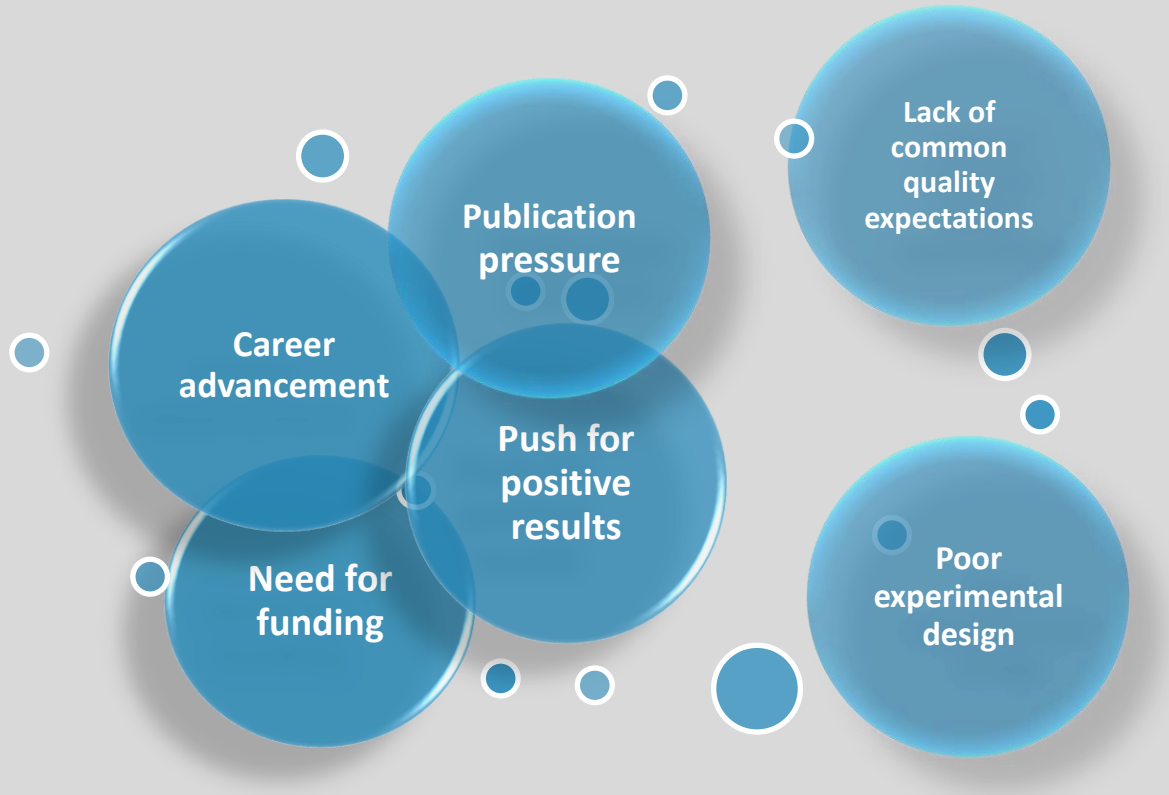
Discovery Data Integrity (DDI) Journey



- Growing number of concerning publications
- Company strategy moved to more emphasis on external innovation

Drivers for poor quality are complex



Multiple players in the field: Pharma, Biotech, Academia, Publishers, Funding agencies, …

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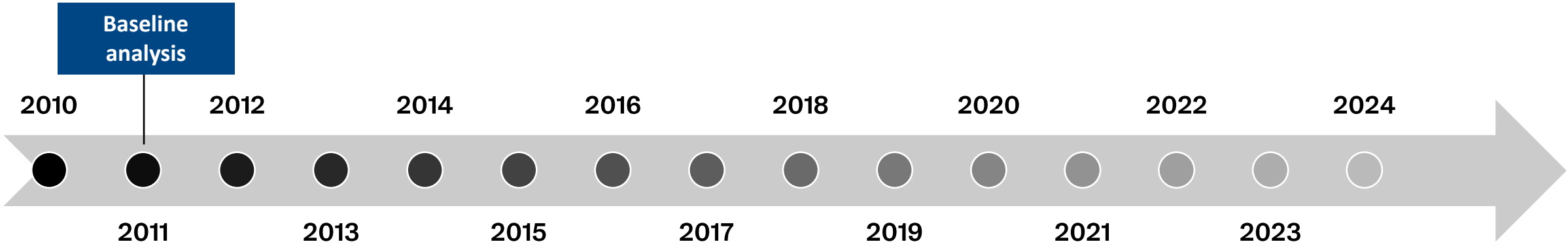


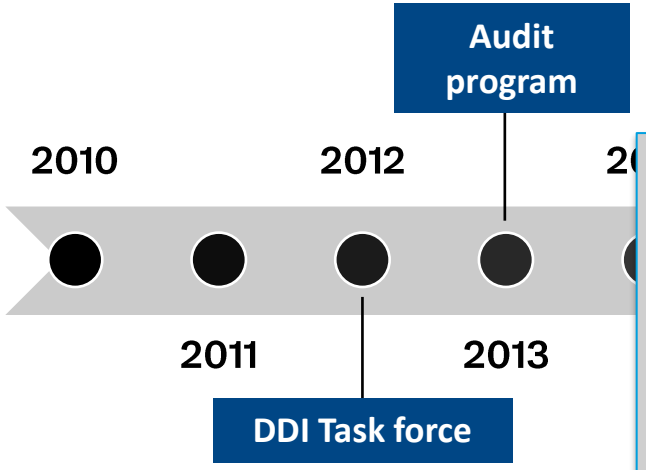
Gaps identified across various locations/business groups

- Variety of data management systems and processes, some more adequate than others
- Unclear storage policies
- Opportunity to improve cross referencing/linking data for easy retrieval

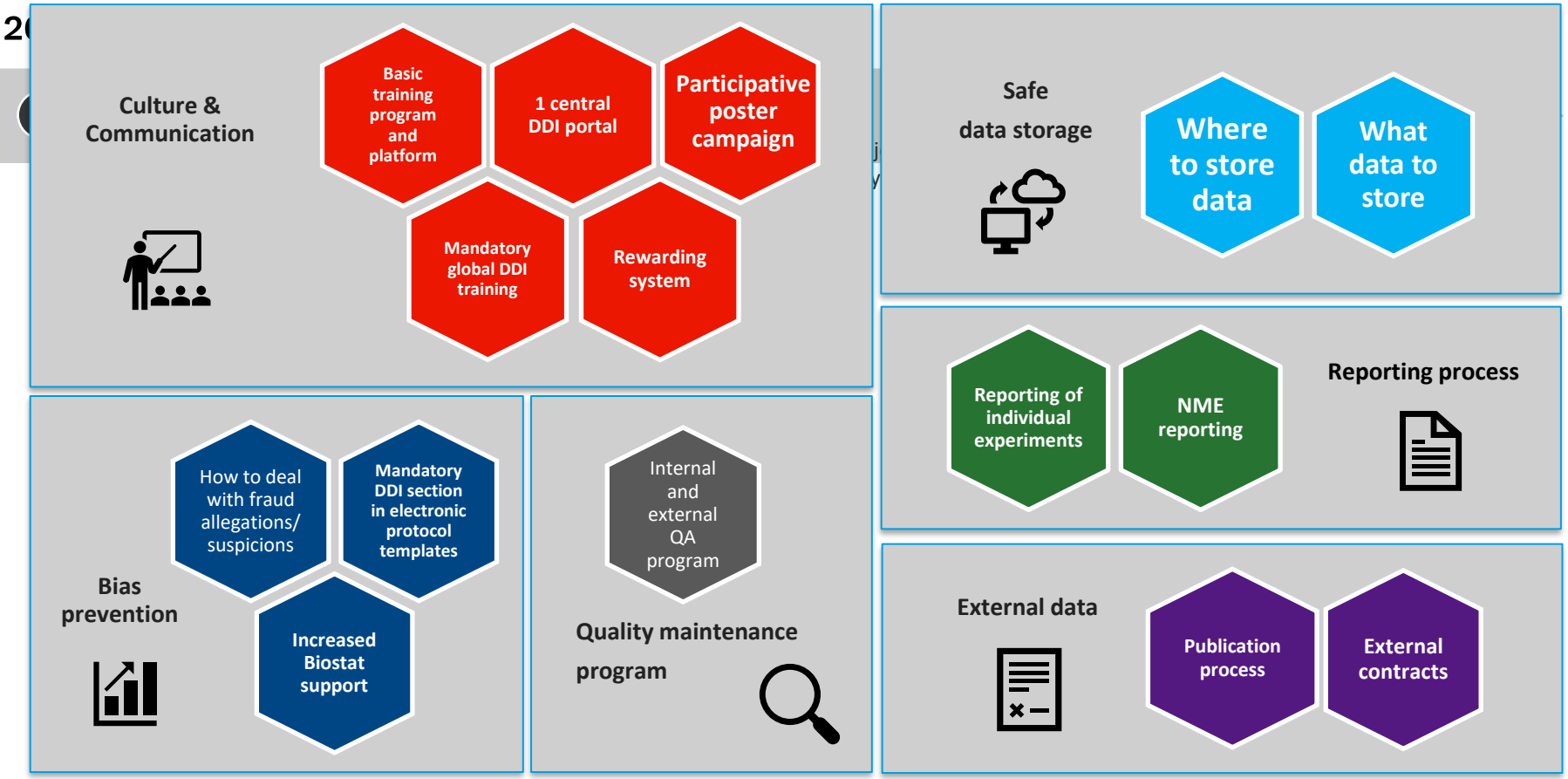
Momentum for change:

- Highly motivated scientists eager to share best practices
- Cross-functional collaboration started to happen immedeately to improve systems

Discovery Data Integrity (DDI) Journey



- 15 DDI workstreams
- Multidisciplinary teams
- Led by Core team
- Sponsored by Senior Leaders
- Culture and communication was prioritized



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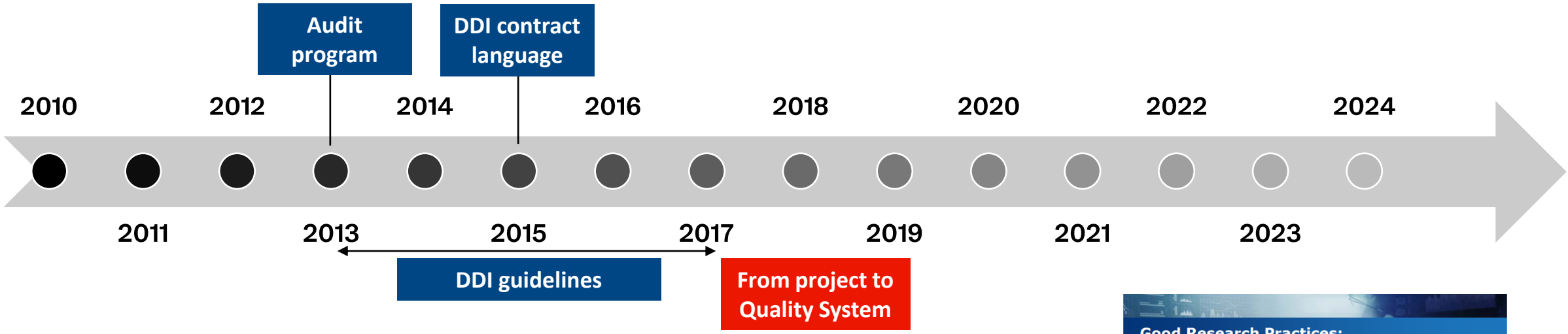

- Experimental records
- NME declaration
- External collaborations

For scientists by scientists

Good Research Practices:
Janssen's Expectations for Collaborators

Janssen is providing the following experimental record-keeping guidelines for organizations to consider when performing non-regulated research under contractual agreement with Janssen. The practices outlined are intended to safeguard data traceability and data integrity, to facilitate decision making and create reliable scientific evidence to bring the best possible solutions to patients. Experimental records must be accurate and thorough enough to trace and reproduce the work that was conducted. These guidelines apply to all personnel who generate, analyze, review, or report data under contractual agreement with Janssen.

Experimental Record Content

- Unique identifiers, such as a lab notebook page reference, should be used for each experiment.
- Each experimental record should contain or cross-reference the names of all scientists involved, objectives, procedures, methods, materials, equipment, dates, and any other details that would allow for reproducibility and reconstruction.
- All data must be captured or cross-referenced, including any raw and processed data.

Storage and Traceability

- Experimental records should be kept in an audit-trailed, version-controlled, safe storage environment such as an appropriate bound-paper laboratory notebook with permanent ink or an electronic laboratory notebook (ELN).
- If bound-paper lab notebooks are used, a separate one should be used solely for work under each Janssen contract.

Data Analysis

- Include sufficient detail to reconstruct any analysis performed, and record all process steps and calculations used.
- Minimize the risk for bias by including criteria for outlier exclusion, acceptable ranges for standards, reference compound and quality controls up-front in the study protocol.
- An experimental record should describe any deviation from a standard protocol and provide a meaningful explanation for exclusion of any data points during analysis.

Review & IP Protection

- Scientific/informal review for completeness and accuracy is advised after recording experimental records.
- Signature by the responsible researcher and signature by a witness should be done within 30 days after completion of the experimental record.

Reporting

- Summarize all related data, processes, and conclusions.
- Include justification for excluding any relevant experimental records or individual data points from the summary analyses.
- Identify all contributing researchers and reference unique identifiers for the experimental records.

For more information or to receive the complete "GUIDANCE FOR JANSSEN'S CONTRACTORS AND COLLABORATORS ON EXPERIMENTAL RECORD-KEEPING FOR NON-REGULATED RESEARCH" please reach out to your Janssen contact

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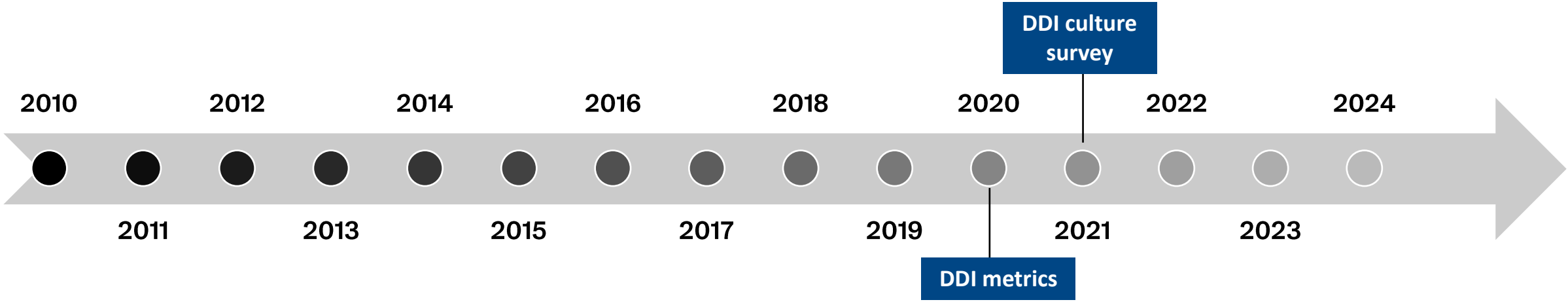
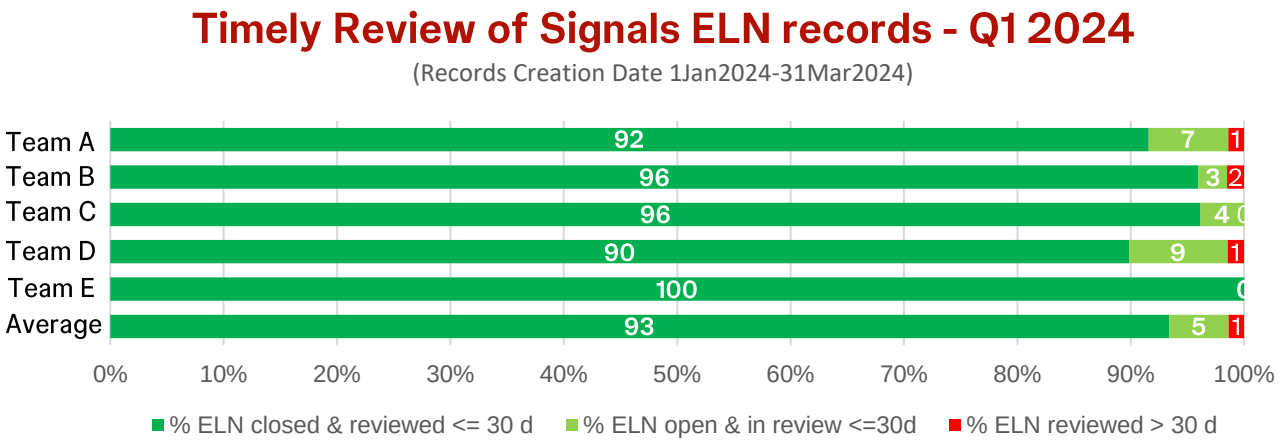
Discovery Data Integrity (DDI) Journey



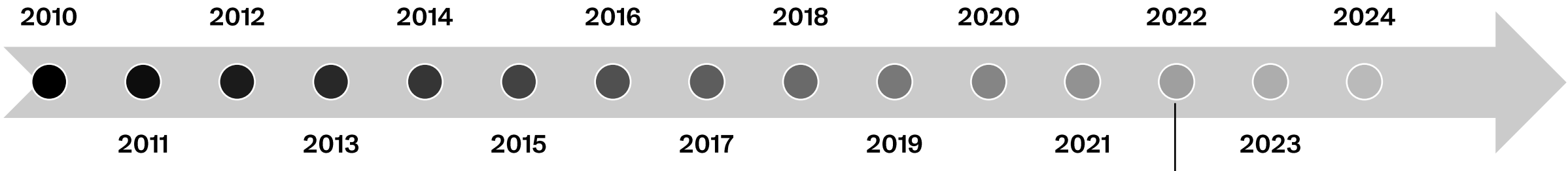


Compliance to:

- Electronic lab notebook timelines
- DDI training taken on time

In addition to spot check audits

Discovery Data Integrity (DDI) Journey



Strengthen DDI champions network

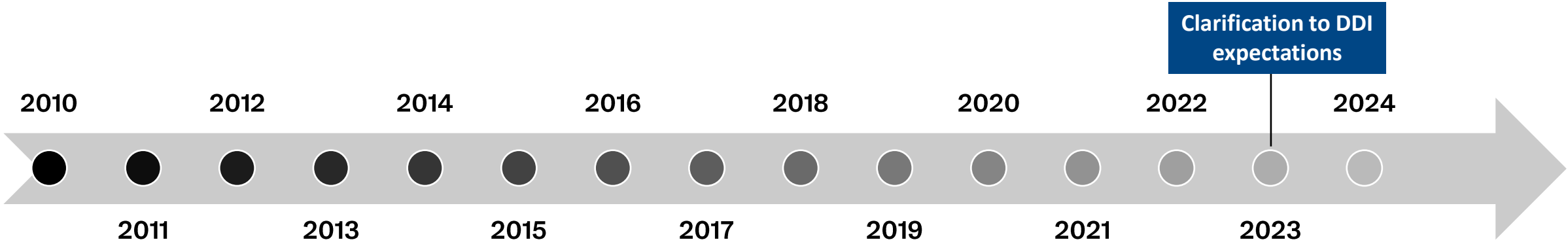
- Active community of ~60 DDI champions
- Clear roles and responsibilities

- Act as **DDI go-to person** for functional team(s).
- Help increase awareness and understanding of DDI through ongoing **communication**. e.g., bring discussions about the importance of DDI within own team, set DDI as a recurrent topic on team meetings in collaboration with team leadership.
- Ensure **alignment with supervisor** on time commitment.

- Facilitate bringing DDI into practice with **fit for purpose approaches**, e.g., reporting templates, proactively ensuring DDI adherence upon implementing new workflows or systems.
- **Participate actively** in DPDS **DDI champions meetings, focus teams** and in **fact-finding exercises**, by sharing expertise, concerns and ideas.

- Ensure new team members have the resources needed on DDI expectations, e.g., remind them of timely completion of DDI training.
- Interpret and follow up on **quarterly DDI Scorecard** and **Training-Compliance metrics**, analyze root causes of poor compliance, take necessary actions in close collaboration with group leaders and communicate within functional teams.

Discovery Data Integrity (DDI) Journey



Report Author
Upon signing the report, a report author is **accountable for the following:**
1. All underlying experimental records are completed and adequately reviewed (additional review for experimental records going into NME or submission may be needed)
2. Report content is consistent within the report and with data in underlying experimental records
3. Report contains complete and correct cross references to underlying experimental records

- Clear accountabilities for authors and reviewers of experimental records and reports
- Example checklists for reviewers
- How to deal with specific scenario's
  (e.g. overarching experiment with subparts in different teams)
- Examples to illustrate what is meant
  (e.g cross referencing to enable full reconstruction)

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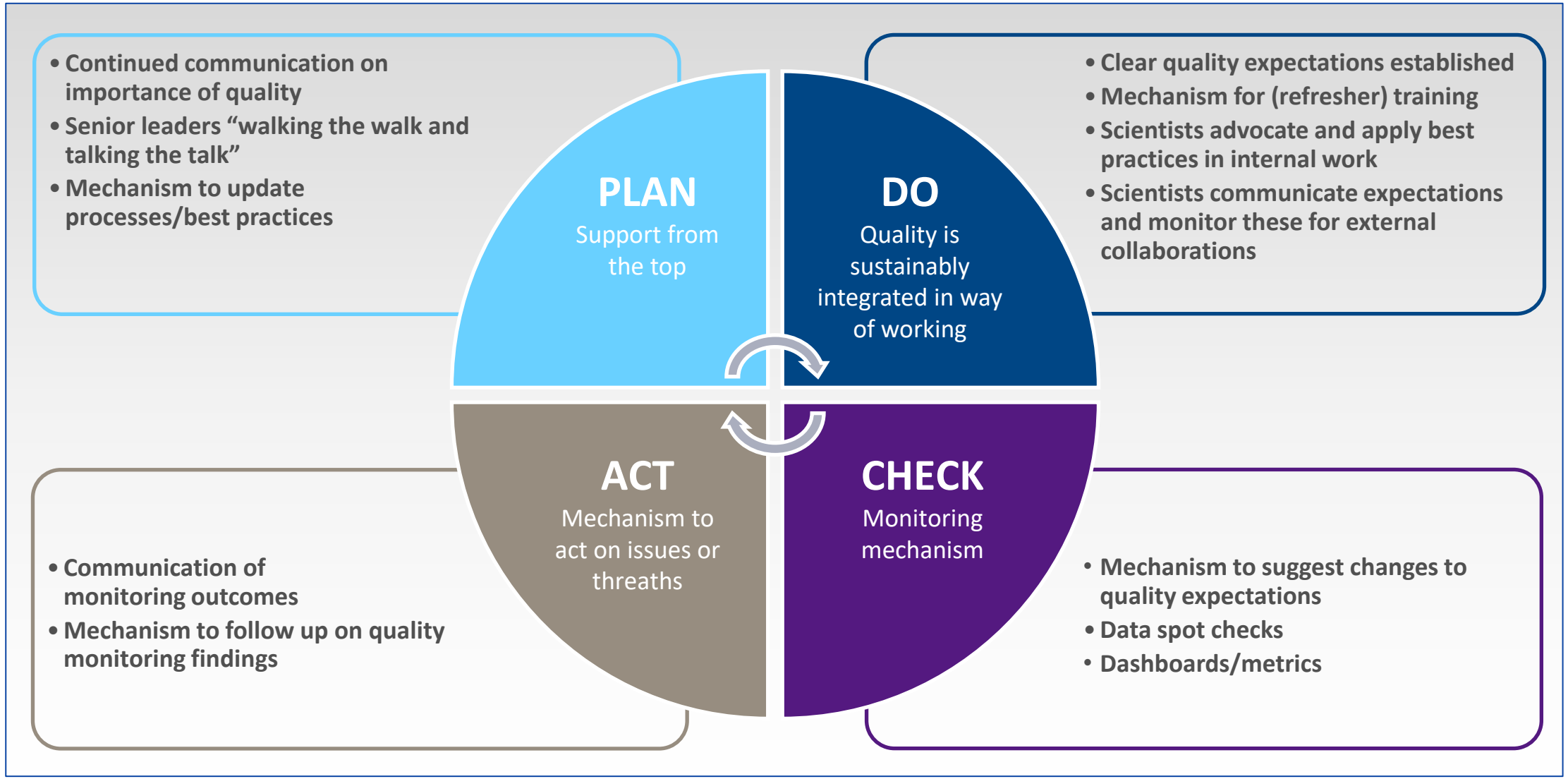
Key Success factors

1. Role Models: Senior leaders' support - "Talking the talk, walking the walk"
2. Mandatory education for all staff (Why? Examples!)
3. Positive Quality culture program (DDI champions, participative poster campaigns, awards)
4. Partnership: Scientists, Quality, IT, Biostatisticians, Legal, Communications, ...
5. Simple, sustainable solutions and "fit for purpose" guidance, "by scientists for scientists"
6. Transparency as central theme: e.g. central data sharing
7. Spot check program and metrics (= measure of success)
8. Speak up culture (hotline)

Characteristics of a mature Quality System



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Usefull resources – Freely accessible online

SOPs4RI

2 Sections → 15 Topics → 131 Tools

- Tools to develop Research Integrity Promotion Plans
- Research Performing & Research Funding organizations

https://sops4ri.eu

EQIPD

Enable → Establish → Maintain

- 18 Core requirements developed by experts from academia and industry
- Stepwise implementation of fit for purpose Quality System in Research

https://go-eqipd.org/about-eqipd/eqipd-quality-system/

Thank you!

Image: *Live cell spinning disk confocal micrograph of C4-2B prostate cancer cell line treated with an investigational biotherapeutic antibody*

Credit: *Brian Stoveken, Discovery Technologies & Molecular Pharmacology, Therapeutics Discovery*